Dual epithelial and immune cell function of Dvl1 regulates gut microbiota composition and intestinal homeostasis.

Journal: JCI Insight

Publication Year: 2016

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PubMed link: 27525310

Funding Grants: Stem cell therapy for inflammatory bowel disease

Public Summary:
Homeostasis of the gastrointestinal (GI) tract is controlled by complex interactions between epithelial and immune cells and the resident microbiota. Here, we studied the role of Wnt signaling in GI homeostasis using Disheveled 1 knockout (Dvl1 -/-) mice, which display an increase in whole gut transit time. This phenotype is associated with a reduction and mislocalization of Paneth cells and an increase in CD8+ T cells in the lamina propria. Bone marrow chimera experiments demonstrated that GI dysfunction requires abnormalities in both epithelial and immune cells. Dvl1 -/- mice exhibit a significantly distinct GI microbiota, and manipulation of the gut microbiota in mutant mice rescued the GI transit abnormality without correcting the Paneth and CD8+ T cell abnormalities. Moreover, manipulation of the gut microbiota in wild-type mice induced a GI transit abnormality akin to that seen in Dvl1 -/- mice. Together, these data indicate that microbiota manipulation can overcome host dysfunction to correct GI transit abnormalities. Our findings illustrate a mechanism by which the epithelium and immune system coregulate gut microbiota composition to promote normal GI function.

Scientific Abstract:
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